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10/598,122	08/18/2006	Sang Min Kim	87914.00002	1310

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EXAMINER	
BROWE, DAVID	
ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,122	KIM ET AL.	
	Examiner	Art Unit	
	DAVID M. BROWE	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to Applicant's timely reply filed September 2, 2010 to the Non-final Office Action of June 2, 2010. No claims have been amended, cancelled or newly added. Claims 1-17 are pending in the application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leonard *et al.* (U.S. Patent Application Pub. No. 2002/0028242), in view of Prater *et al.* (U.S. Patent Application Pub. No. 2004/0052846) and Karehill *et al.* (U.S. Patent No. 6,605,303).

Applicant Claims

Applicants claim a sustained-release tablet with a) a core comprising paroxetine, b) a separation layer that completely encloses the core comprising a water-insoluble polymer and/or a water-soluble polymer, and c) an enteric coating layer. The paroxetine is paroxetine hydrochloride hemihydrate. The core weight is comprised of 40-90 wt% paroxetine-containing granules, the granule weight comprised of 3-30 wt% high-viscosity hydroxypropyl methylcellulose and 10-40 wt% low-viscosity hydroxypropyl methylcellulose, with viscosity ranges of 3,000-14,000 cps and 40-60 cps, respectively; and further comprises low-viscosity hydroxypropyl methylcellulose and other pharmaceutically acceptable binders and excipients. The separation layer comprises 1-30 wt%, based on the weight of the tablet core; and is prepared from at least one water-insoluble polymer selected from the group consisting of ethylcellulose, polyvinyl acetate, and ammoniomethacrylate copolymer type B; and/or at least one water-soluble polymer selected from the group consisting of hydroxypropyl methylcellulose, methylcellulose, polyvinylpyrrolidone, ammoniomethacylate copolymer type A, and polyvinyl alcohol. The enteric coating layer is prepared from a polymer selected from the group consisting of

methacrylate copolymer, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate phthalate, cellulose acetate phthalate and carboxymethylethylcellulose.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Leonard *et al.* disclose a sustained-release tablet with *a)* a core comprising paroxetine; and *b)* an enteric coating layer (Pg. 1, secs. 0001, 0004-0005, 0007-0008, 0014, 0018; Pg. 2, secs. 0023, 0050). The paroxetine is paroxetine hydrochloride hemihydrate (Pg. 2, sec. 0023). The core contains high-viscosity hydroxypropyl methylcellulose and low-viscosity hydroxypropyl methylcellulose, with viscosity ranges of 3,000-14,000 cps and 40-60 cps, respectively; and further comprises other pharmaceutically acceptable binders and excipients (Pg. 2, sec. 0049). The enteric coating layer is prepared from a polymer selected from the group consisting of methacrylate copolymer, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate phthalate, cellulose acetate phthalate and carboxymethylethylcellulose (Pg. 2, sec. 0050; Pg. 3, sec. 0051).

Prater *et al.* disclose a sustained-release tablet with *a)* a core comprising an active agent, *b)* a separation layer that completely encloses the core comprising a water-insoluble polymer and/or a water-soluble polymer, and *c)* an enteric coating layer (Pg. 2, secs. 0020-0022, 0024, 0028-0029, 0031; Pg. 3, secs. 0032-0034, 0040, 0043; Pg. 4, sec. 0056). The core can comprise 5-80 wt% of any one of numerous types of active agents; and further comprises hydroxypropyl methylcellulose and other pharmaceutically acceptable binders and excipients (Pg. 2, secs. 0029, 0031; Pg. 3,

sec. 0043; Pg. 6, sec. 0094). The separation layer comprises 1-30 wt%, based on the weight of the tablet core; and is prepared from at least one water-insoluble polymer selected from the group consisting of ethylcellulose, polyvinyl acetate, and ammoniomethacrylate copolymer type B; and/or at least one water-soluble polymer selected from the group consisting of hydroxypropyl methylcellulose, methylcellulose, polyvinylpyrrolidone, ammoniomethacylate copolymer type A, and polyvinyl alcohol (Pg. 2, secs. 0021; Pg. 3, secs. 0032-0034; Pg. 9, secs. 0151-0152). The enteric coating layer is prepared from a polymer selected from the group consisting of methacrylate copolymer, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate phthalate, cellulose acetate phthalate and carboxymethylethylcellulose (Pg. 8, sec. 0145).

Karehill *et al.* disclose a sustained-release tablet with *a)* a core comprising an active ingredient, *b)* a separation layer that completely encloses the core, and *c)* an enteric coating layer (Col. 1, lns. 8-13; Col. 3, lns. 25-29, 55-67; Col. 4, lns. 1-5). The core is composed of active granules with granule weight comprised of 3-30 wt% high-viscosity hydroxypropyl methylcellulose and 10-40 wt% low-viscosity hydroxypropyl methylcellulose, with viscosity ranges of 3,000-14,000 cps and 40-60 cps, respectively (Col. 16, lns. 5-15); and further comprises other pharmaceutically acceptable binders and excipients (Col. 4, lns. 13-15, 28-30). The separation layer comprises 1-30 wt%, based on the weight of the tablet core; and is prepared from at least one water-insoluble polymer selected from the group consisting of ethylcellulose, polyvinyl acetate, and ammoniomethacrylate copolymer type B; and/or at least one water-soluble polymer

selected from the group consisting of hydroxypropyl methylcellulose, methylcellulose, polyvinylpyrrolidone, ammoniomethacylate copolymer type A, and polyvinyl alcohol (Col. 9, lns. 46-48, 56-62). The enteric coating layer is prepared from a polymer selected from the group consisting of methacrylate copolymer, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate phthalate, cellulose acetate phthalate and carboxymethylethylcellulose (Col. 10, lns. 13-20).

Ascertainment of the Difference Between the Scope of the Prior Art and the Claims (MPEP §2141.012)

Leonard *et al.* do not explicitly disclose that a sustained-release tablet comprising paroxetine and an enteric coating can further comprise a separation layer containing at least one water-insoluble polymer and at least one water-soluble polymer, and that the paroxetine granules in the core specifically comprise 3-30 wt% high-viscosity hydroxypropyl methylcellulose and 10-40 wt% low-viscosity hydroxypropyl methylcellulose, with viscosity ranges of 3,000-14,000 cps and 40-60 cps, respectively. These deficiencies are cured by the teachings of Prater *et al.* and Karehill *et al.*

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of the present invention to combine the respective teachings of Leonard *et al.*, Prater *et al.*, and Karehill *et al.* to arrive at applicants' claimed sustained-release tablet.

Leonard *et al.* disclose that a controlled-release formulation comprising paroxetine-containing cores surrounded by an enteric coating affords an unexpected

reduction in the side effects, such as nausea, often experienced by patients administered conventional immediate-release formulations of paroxetine (Pg. 1, secs. 0004-0005, 0007, 0017; Pg. 2, sec. 0050). However, a controlled-release formulation based solely on an enteric coating of a drug-containing core is dependent on the gastric emptying time (GET) (Prater *et al.*, Pg. 2, sec. 0016). Since Prater *et al.* disclose that a controlled-release formulation with a separation layer between the core and the enteric coating that completely encloses the core and comprises a water-insoluble polymer and/or a water-soluble polymer is capable of controlled-release of active agent without regard to the effect of GET or other GI tract parameters such as the fed/fast state (Pg. 2, secs. 0018-0019, 0021; Pg. 3, secs. 0032-0033, 0047; Pg. 4, sec. 0056); and Karehill *et al.* disclose that formulating an active agent in core granules that specifically contain 3-30 wt% high-viscosity hydroxypropyl methylcellulose and 10-40 wt% low-viscosity hydroxypropyl methylcellulose, with viscosity ranges of 3,000-14,000 cps and 40-60 cps, respectively, affords a facilitated extended-release drug plasma profile (abstract; Col. 1, lns. 8-13; Col. 2, lns. 24-27; Col. 16, lns. 5-15); one of ordinary skill in the art would be motivated to formulate the sustained-release paroxetine tablet of Leonard *et al.* with the said separation layer between the core and enteric coating, and with a core containing paroxetine granules comprising 3-30 wt% high-viscosity hydroxypropyl methylcellulose and 10-40 wt% low-viscosity hydroxypropyl methylcellulose, having viscosity ranges of 3,000-14,000 cps and 40-60 cps, respectively, with the reasonable expectation that the resulting tablet will successfully provide constant, sustained paroxetine release with reduced side effects and without regard to the GET.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments filed September 2, 2010 have been fully considered but they are not persuasive.

i) Applicants assert that "*Applicant's claimed invention aims to provide a tablet having a constant release pattern rather than simply having a sustained-release or a delayed-release pattern*".

Respectfully, however, the Examiner cannot agree. Applicants' claims are directed to "An enteric, sustained-release tablet"; and although applicants specify that the drug release behavior does not depend on the residence time of the drug in an acidic environment, nowhere do applicants explicitly claim that the tablet has a constant release pattern.

ii) Applicants assert that "*Prater does not disclose the sustained release technology*"; that "*Prater discloses a delayed-release formulation, not a controlled release formulation*".

Respectfully, however, the Examiner would like to point out that the 35 USC 103 rejection of claims 1-17 is based on a combination of the respective teachings of Leonard *et al.*, Prater *et al.*, and Karehill *et al.*, and not just on the teachings of Prater *et al.* alone. Indeed, Leonard *et al.*, Prater *et al.*, and Karehill *et al.* each teach a controlled release formulation. Although Prater prefers tablets that exhibit a delayed and then rapid release of the drug, Prater also discloses other tablet embodiments that exhibit controlled drug release for up to 12 hours (see, for example, Pg. 3, sec. 0040). Moreover, Prater *et al.* and Karehill *et al.* each disclose not only controlled-release, but also a tablet structure that comprises a core containing the active agent, a separation layer completely enclosing the core containing at least one water-insoluble polymer, such as ethylcellulose, and/or at least one water-soluble polymer, such as hydroxypropylmethylcellulose; and an enteric coating.

iii) Applicants assert that "*the regulatory membrane coating disclosed by Prater is a replacement of a conventional enteric coating layer*"; and "*In Prater, no separation layer is introduced between the core and the outer coating (the regulatory membrane coating)*"; and "*the regulatory membrane coating disclosed by Prater is merely a replacement of a conventional enteric coating*".

The Examiner, however, would like to point out that Prater first describes dosage forms comprising the core and the "regulatory layer" completely enclosing the core containing at least one water-insoluble polymer, such as ethylcellulose, and/or at least one water-soluble polymer, such as hydroxypropylmethylcellulose; then Prater *et al.* subsequently go on to disclose that "formulations of this invention ...will typically have

an additional, enteric coat" (see Pg. 4, sec. 0056), and that this enteric coat is added on top of the "regulatory layer" and serves a unique function in ensuring colonic delivery of the active agent. In effect, the "regulatory layer" becomes the "separation layer" between the core and the enteric coat, and does not represent a replacement for the enteric coat.

iv) Applicants assert that "*there is no motivation described in the cited references to induce the separation layer in order to solve the problem when the enteric coating is directly introduced on the core*".

The Examiner, however, would like to point out that the motivation to combine references is clearly stated in the 103 rejection presented in the Non-final Office Action of June 2, 2010. Thus, in part, Prater *et al.* disclose that controlled-release formulations in which a core containing active agent is surrounded by only an enteric coating are dependent on the GET (Pg. 2, sec. 0016); that this is a disadvantage, and that a goal is the development of a system which is independent of the physiological condition of the GI tract, unaffected by the fed/fast condition (Pg. 2, sec. 0018); and that the dependence on GET can be overcome by the "regulatory layer" completely enclosing the core (Pgs. 3-4 secs. 0043, 0047).

For the aforementioned reasons, and the reasons already of record, the 35 U.S.C. § 103 rejection of claims 1-17 is hereby maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID M. BROWE whose telephone number is 571-270-1320. The examiner can normally be reached on Monday-Friday 7:30AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Carlos A. Azpuru/
Primary Examiner, Art Unit 1617

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